UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,650	01/19/2006	Masanori Kobayashi	50026/050001	4242

21559 7590 12/01/2006

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
MAKAR, KIMBERLY A	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/526,650	KOBAYASHI ET AL.	
	Examiner	Art Unit	
	Kimberly A. Makar	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03/03/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase "derived from" which is not clearly defined in the claim nor in the specification. Dos this refer to a neuraminidase that literally comes from (is purified from) a Gram-positive bacterium? Or, an amino acid sequence with 100 % homology to a neuraminidase? If a neuraminidase is derived from an alternate source (ie Gram-negative bacterium) and is mutated to have 100% homology to a Gram-positive neuraminidase, would this then still be considered "derived from"? What if the homology is not 100%, but 95%? 85%? A skilled artisan would be unable to determine the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 5-10, and 14-18 are rejected under 35 U.S.C. 102(b) as being taught by Bates et al (WO 99/13905) listed in applicants IDS 1449 form dated 07/13/05. Claims 1, 5-10, and 14-18 recite a method for producing a viral vector comprising a membrane protein that binds to sialic acid, comprising the steps of culturing the viral vector in the presence of a neuraminidase derived from a Gram-positive bacterium, and recovering the produced virus (claim 1). The method is further limited wherein the viral vector is a retroviral vector (claim 5) and wherein the retroviral vector is a lentiviral vector (claim 6). The method is further limited wherein the membrane protein that binds to sialic acid is an envelope protein of a single strand negative RNA virus (claim 7), wherein the single strand negative RNA virus is of the Paramyxoviridae or Orthomyxoviridae family (claim 8). The method is further limited wherein the membrane protein is an HA protein from an influenza virus (claim 9). Claims 10 recites a virus produced according to claim 1. Claim 14 recites a virus according to claim 5. Claim 15 recites a virus according to claim 6. Claim 16 recites a virus according to claim 7. Claim 17 recites a virus according to claim 8. Claim 18 recites a vector according to claim 9.

3. Bates et al (WO 99/13905) listed in applicants IDS f1449 form dated 07/13/05 teaches a method of for producing Murine Leukemia Viruses (MLV) pseudotyped with influenza A hemagglutinin (HA). Specifically, he teaches the method to produce the pseudotyped viruses in culture (page 24, lines 20- page 25 lines 13). Bates teaches that while the preferred embodiment of the virus is MLV, other retroviruses and lentiviruses are additional embodiments for pseudotyping (page 12, lines 1-5). Additionally, while Bates teaches the production of mutant HA proteins that do not bind

sialic acid, he teaches the production of the wild type influenza HA protein that does bind sialic acid as a control (see figure 3A) and states that the HA molecule is "from influenza A virus and mutants there of" (page 13, line 5). Furthermore, Bates teaches the production of the pseudotyped virus comprising the influenza A HA protein that binds sialic acid by culturing 293 T cells in the presence of neuraminidase derived from *Clostridium perfringens*, a Gram-positive bacteria. Bates teaches the methods of production of, and the viruses derived from the production of those methods. Thus Bates teaches the claimed invention.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2-4, 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bates et al (WO 99/13905) listed in applicants IDS f1449 form dated 07/13/05 and Luo et al (US Patent No: 5,714,509) in view of Hasegawa et al (US Patent No: 5,268,290). Claims 2-4, 11-13 recite a method for producing a viral vector comprising a membrane protein that binds to sialic acid, comprising the steps of culturing the viral vector in the presence of a neuraminidase derived from a Gram-positive bacterium, and recovering the produced virus (claim 1). The method is further limited wherein the Gram-positive bacterium is an actinomycete (claim 2) of the family of *Micromonospora*

viridifaciens (claims 3 and 4). Claim 11 recites a virus according to claim 2. Claim 12 recites a virus according to claim 3. Claim 13 recites a virus according to claim 4.

6. Bates et al (WO 99/13905) listed in applicants IDS f1449 form dated 07/13/05 teaches a method of producing a viral vector comprising a membrane protein influenza A HA protein that binds to sialic acid, comprising culturing cells producing the vial vector in the presence of a neuraminidase derived from a Gram-positive bacterium and recovering the produced virus (see above). Bates does not teach that the Gram-positive bacterium is an actinomycete *Micromonospora viridifaciens*.

7. Luo at al (US Patent 5,714,509) teaches that neuraminidases (also known as sialidases) derived from bacteria are highly homologous, with a sub-group of sialidases comprising *Clostridium perfringens*, *Clostridium sordelli*, *Micromonospora viridifaciens*, and *Salmonella typhimurium* having a very high degree of homology to each other. Luo teaches that this sub-group has sialidases that do not require metal ions for activity, and that the *Salmonella typhimurium* has a structural fold that is the same as the influenza neuraminidase (see column 1, line 44 through column 2, lines 7).

8. Hasegawa et al (US Patent No: 5,268,290) teaches a method of producing large volumes of neuraminidase derived from *Micromonospora viridifaciens* (see abstract). Hasegawa teaches that an advantage to his system is that it "produces neuraminidase at lost costs in an industrial scale" and does not require "supplementing any neuraminidase inducer" (Column 1, lines 35 – 64, particularly lines 45-56).

9. A skilled artisan at the time the invention was made would have been motivated to combine the teaching of Bates on a method of producing a viral vector comprising a

membrane protein influenza A HA protein that binds to sialic acid, comprising culturing cells producing the vial vector in the presence of a neuraminidase derived from a Gram-positive bacterium and recovering the produced virus with the teaching of Luo et al, on the high homology of the neuraminidases derived from the sub-group of *Clostridium perfringens*, *Clostridium sordelli*, *Micromonospora viridifaciens*, and *Salmonella typhimurium,* which has a active site with high homology to the influenza A neuraminidase that do not require inducers, further with the teaching of Hasagawa on a method of producing large volumes of neuraminidase derived from *Micromonospora viridifaciens* at low cost and without inducers because altering the methodology of Bates by producing the neuraminidase derived from *Clostridium perfringens* with a neuraminidase derived from *Micromonospora viridifaciens* would reduce the cost of producing the pseudotyped viruses, and would ensure that the new pseudotyped viruses would still be able to bind the exchange neuraminidase derived from *Micromonospora viridifaciens,* since it has been shown to have such a high homology to the neuraminidase derived from *Clostridium perfringens.* It would have been obvious to the skilled artisan to combine the teaching of Bates on a method of producing a viral vector comprising a membrane protein influenza A HA protein that binds to sialic acid, comprising culturing cells producing the vial vector in the presence of a neuraminidase derived from a Gram-positive bacterium and recovering the produced virus with the teaching of Luo et al, on the high homology of the neuraminidases derived from the sub-group of *Clostridium perfringens*, *Clostridium sordelli*, *Micromonospora viridifaciens*, and *Salmonella typhimurium,* which has a active site with high homology to the influenza A

neuraminidase that do not require inducers, further with the teaching of Hasagawa on a method of producing large volumes of neuraminidase derived from *Micromonospora viridifaciens* at low cost and without inducers because altering the methodology of Bates by producing the neuraminidase derived from *Clostridium perfringens* with a neuraminidase derived from *Micromonospora viridifaciens* would reduce the cost of producing the pseudotyped viruses, and would ensure that the new pseudotyped viruses would still be able to bind the exchange neuraminidase derived from *Micromonospora viridifaciens,* since it has been shown to have such a high homology to the neuraminidase derived from *Clostridium perfringens.* Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had reasonable expectation of success in practicing the claimed invention.

Conclusion

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

kam/11/24/06

DAVID GUZO
PRIMARY EXAMINER